BREVE 25

ACCESS, DEVELOPMENT, AND ECONOMIC REGULATION OF THE PHARMACEUTICAL MARKET IN BRAZIL

Brief based on the webinar presented by Leandro Safatle on 26 March (2019) in Red CRITERIA.

1. INTRODUCTION

Health expenditure is growing much faster than income virtually all around the world. This is due to many factors, including the demographic and epidemiological transition, higher middle-class expectations, and, primarily, the existence of more and better health technologies such as pharmaceuticals and medical devices. The latter is estimated to account for 25%-75% of countries' growth in health expenditure (Sorenson, Drummond and Bhuiyan Khan 2013) (Rao, et al. 2021).

Brazil is not exempt from the general rule. Pharmaceutical expenditures rose from R$14.3 billion in 2010 to R$20 billion in 2015, a 40% increase. This expenditure currently represents 16% of the public health budget (Sulpino Vieira 2018).

To meet this challenge, Brazil has been implementing a series of policies such as the regulation of pharmaceutical prices. This policy brief outlines the main strategies that the country has introduced and the outcomes to date. It also discusses the importance of regulatory designs aligned with country policy objectives and the local context and argues that well designed regulations can benefit all actors, including the government, the public, and the pharmaceutical industry.

1.1 WHY REGULATE PHARMACEUTICAL PRICES?

The pharmaceutical market is highly imperfect, marked by numerous information asymmetries, many barriers to the entry of new competitors, and the existence of monopolistic micromarkets (Rattinger, et al. 2008). In this context, regulation – and more specifically, price regulation – is critical for controlling costs and monopoly power (Kanavos 2016). That is why countries with highly consolidated market economies, such as New Zealand, England, Australia, Canada, Japan, and Sweden, have systematically turned to price regulation.

1.2 MAIN PHARMACEUTICAL MARKET IMPERFECTIONS

To understand the reasons for regulating pharmaceutical prices, it is necessary to know about the imperfections in the pharmaceutical market, including information asymmetries, principal-agent problems, and monopolistic tendencies.

Information asymmetries. Health workers possess technical knowledge about pharmaceuticals, but patients do not. Since patients need a health professional to prescribe the pharmaceuticals they need, prescription pharmaceuticals are considered credentialed products[1]. This information asymmetry is an imperfection that impedes market equilibrium because consumers do not have all the information they need to choose the right pharmaceutical for their illness or to compare quality and price.

Principal-agent problem. In the pharmaceutical market, the patient – the principal economic actor – depends on the action of the doctor – the agent – who has the technical knowledge to prescribe the right pharmaceutical. Since the individual who chooses the pharmaceutical is not the one who has to pay for it, the health professional serves as a substitute consumer, and price does not influence the choice or demand for a particular pharmaceutical. As a result, the supply and demand curves end up converging at a non-optimal point, and the price does not reflect the equilibrium point.

Monopolistic tendency. The market for original patented pharmaceuticals is monopolistic by definition, since there is no exact substitute for them. Pharmaceutical companies can therefore set prices unrelated to the marginal costs. Moreover, pharmaceuticals have a low price elasticity of demand, since they are essential products for treating diseases.

In short, the pharmaceutical market has imperfections that keep free supply and demand in themselves from guaranteeing access to pharmaceuticals by the people

who need them. These imperfections impede consumer sovereignty in the pharmaceutical market, resulting in inequitable and inefficient access. Figure 1 lists other imperfections in the pharmaceutical market[2] along with those already mentioned.

Failure to regulate the pharmaceutical market can have major implications for prices and spending on pharmaceuticals and medical devices. There is evidence indicating that an unregulated pharmaceutical market gives rise to opportunistic behaviors at different points in the supply chain. This in turn creates a series of problems such as, shortages, excessively high prices and low sales, and erratic and harmful behavior in general. (Lopes 2000).

Since pharmaceutical expenditure is a function of price and volume[3] (Expenditure = Prices x Volume), interventions to control pharmaceutical expenditure have been concentrated on influencing price or quantity. This policy brief will specifically address price interventions, which are considered a determinant of access to pharmaceuticals, together with other policies, such as the selection of pharmaceuticals covered by the public system, the rational use of pharmaceuticals, sustainable financing, and reliable supply and health systems.[4]

2. NECESSARY ELEMENTS FOR REGULATION

2.1 SETTING OBJECTIVES

The World Health Organization (WHO) recommends using a combination of policies aligned with the objectives of the health system. These policies should include a legal framework, governance mechanisms, and a suitable administrative structure; be supported by the necessary technical capacity and periodically reviewed and monitored (including prices); and constantly be evaluated and reformulated. The recommended policies include the regulation of margins, tax reductions or exemptions, the use of external reference pricing (also called international reference pricing), the promotion of generics, and the use of health technology assessment (HTA). Figure 2 lists some of the objectives that can be pursued with a regulatory policy.

FIGURE 1 **Consequences of the failure to regulate the pharmaceutical market**

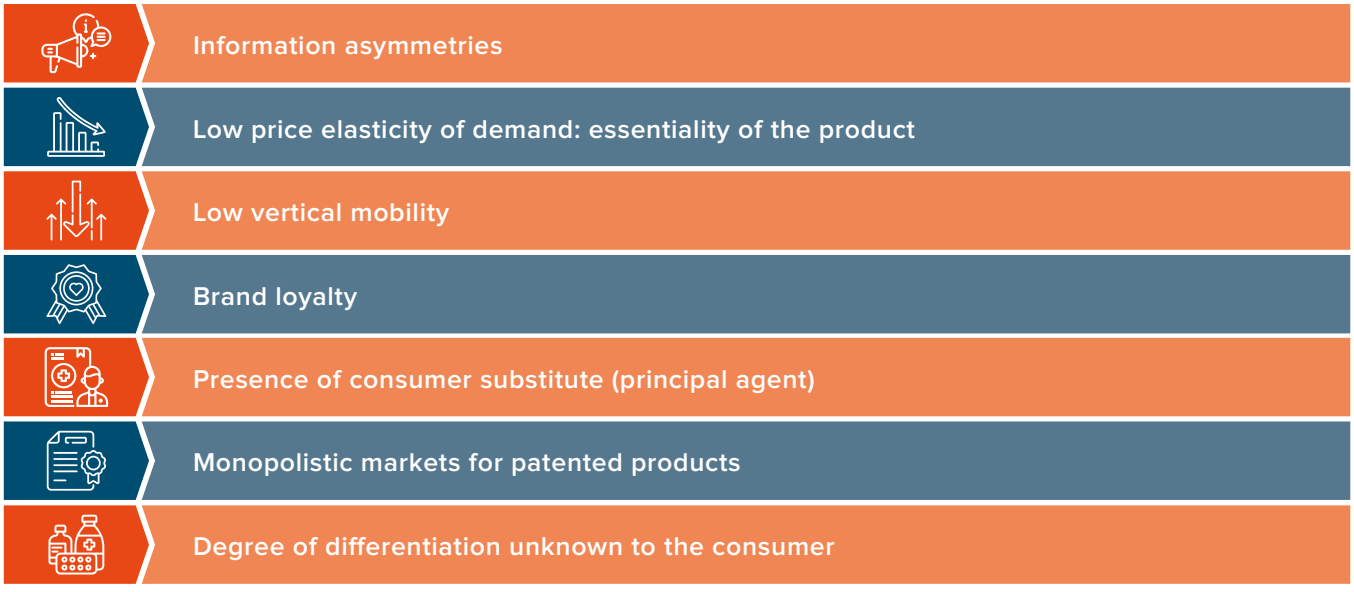


FIGURE 2 Objectives that can be met with economic regulation of the pharmaceutical market

2.2 CONTEXT ANALYSIS

A well-designed regulation requires a comprehensive analysis of the context in which it is to be implemented. A proper analysis of the main problems affecting the market is essential for determining which strategies to adopt, as well as the feasibility and viability of their implementation. There is no such thing as regulatory instruments that are good or bad in themselves, nor is there a universal regulatory design that works in all countries and for all purposes: a study must be conducted that analyzes aspects of the market structure.

One of the most important aspects of the analysis for determining the economic regulatory mechanisms is the country's productive tradition. The less consolidated the domestic pharmaceutical industry, the greater its tendency to produce copy pharmaceuticals – that is, generic, similar, and biosimilar pharmaceuticals. The direct price regulation mechanisms for this type of pharmaceutical may or may not encourage domestic production, which could affect the accessibility of pharmaceuticals. Furthermore, the higher the proportion of this type of medicine as a share of total consumption, the greater the impact of the measure.

FIGURE 3 Dimensions to evaluate before designing regulations

Size and outlook for the domestic market	» What is the country's productive tradition and how has its manufacturing evolved? » What is the degree of imports and how are pharmaceutical imports segmented?
Health system	» How does the public health system work? » How does the social security system work? » What is the relationship between financiers and service providers?
Pharmaceutical procurement processes	» How does public sector pharmaceutical procurement and despensing work? Are there centralized purchasing mechanisms? Are there systems for setting parameters for the introduction of new technologies? Are there price negotiation mechanisms?
Private demand	» How competitive is the retail market and what is the degree of market penetration of generics, bioequivalent and biosimilar pharmaceuticals? » Is there some type of reimbursement program?
Country regulatory and health system	» How is it structured? » How are the safety and efficacy of domestically produced and imported pharmaceuticals guaranteed?
Evaluation of the institutional environment	» What is the composition of the ministries, secretariats, and agencies that act in this market? » Are there public policies to encourage competition, transparency, and the reduction of asymmetries?

Considering the domestic industry's development level and other aspects of the pharmaceutical market, governments have a wide range of regulatory measures to choose from. An appropriate analysis leads to the definition of health regulation strategies that will have an impact on the economic agents. Figure 3 shows some of the dimensions that should be evaluated before designing regulations.

2.3 RELATIONS WITH OTHER SECTORS

Any public policy must consider the impact of regulation on all related sectors. Figure 4 describes these interconnections. The Economic and Industrial Health Complex (CEIS) model proposed for Brazil in the early 2000s illustrates the systems perspective and emphasizes how fundamental it is to regulatory design. This model describes the complementary relationships between the industrial and health sectors when it comes to health policy; the health sector production base must be expanded if there is to be universal health coverage. As Grabois et al. (2012) mention, in this model, the national State must mediate the different interests of the sectors to develop an agenda that produces and integrates technological innovation and reconfigures health systems according to the epidemiological profile of Brazil.

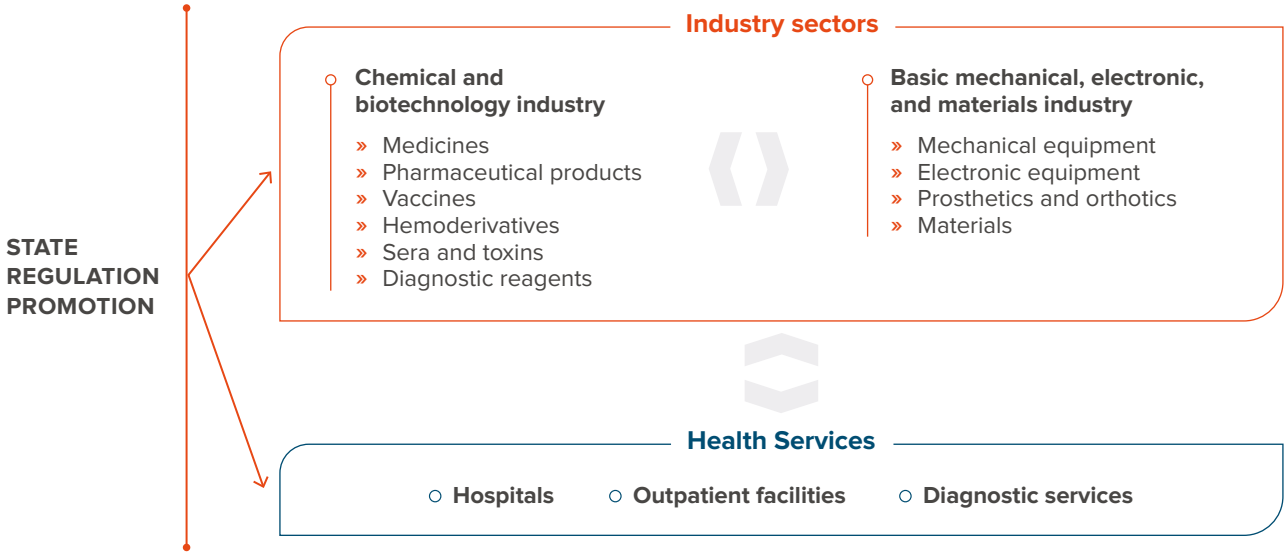
3. THE PRICE REGULATION EXPERIENCE IN BRAZIL

3.1 HISTORY OF REGULATION IN BRAZIL

The pharmaceutical market in Brazil has been regulated for many decades (see Figure 5). In 1950, price ceilings were set (based on cost, benefit, and expenditure), along with an annual price adjustment. The objective of this measure was to lower domestic prices and bring them closer to international parameters, since pharmaceutical prices in Brazil were higher than those in the international market. Price control mechanisms in the following decades were more direct: price freezes (1960) and price tabulations (1970). The 1990s saw tensions between the private sector and the government, because the regulations were inflexible and inefficient. There was a brief attempt to deregulate the market, but the results of this deregulation period were not positive, as the measure gave rise to opportunistic behavior, with prices well above inflation, leading to a drop in sales and access to pharmaceuticals, as well as shortages in the market.

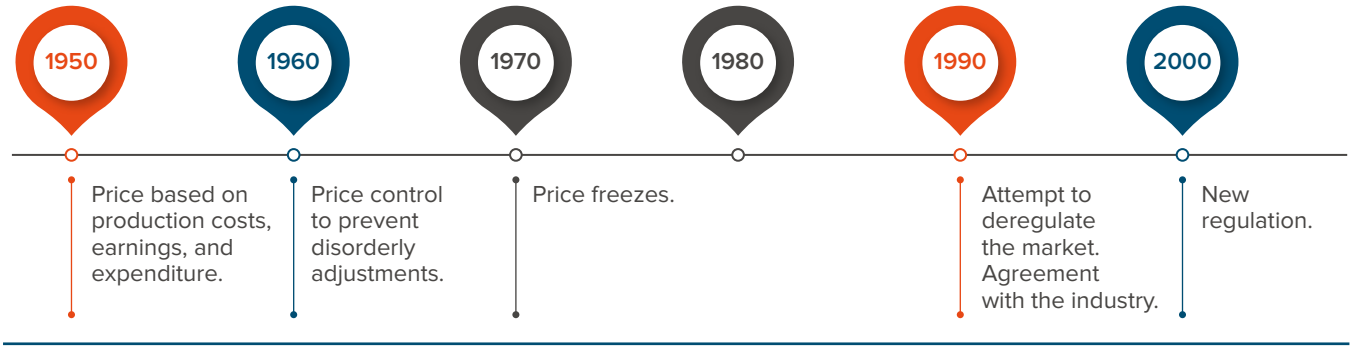
The lack of price control was concerning not only to the Ministry of Health but the Ministry of Economy. With the due motivation, a Parliamentary Commission of Inquiry (Comissão Parlamentar de Inquérito – CPI) was formed to investigate the matter from a legislative standpoint and became a commission to hear testimonies and obtain information directly in response to complaints. As a result of these investigations, in late 1999 the Commission issued a recommendation to regulate the pharmaceutical,

FIGURE 4 Economic and Industrial Health Compound



Source: Grabois Gadelha, Silveira Costa and Maldonado 2012, 23.

FIGURE 5 Milestones in pharmaceutical regulation in Brazil



Source: Febrafarma.

orthotics, and prosthetics markets due to existence of intrinsic market imperfections. In 2000, the National Congress created the Pharmaceutical Chamber (CAMED), following the recommendations to regulate the pharmaceutical market, and the prices of these products have been regulated since then. In 2002, CAMED became the Brazilian Chamber for Regulation of the Pharmaceutical Market (CMED), continuing the regulation of the market. Thus, modern regulation in Brazil dates back more than 20 years.

CMED is made up of four Brazilian federal ministries (Ministry of Health, Ministry of Economy, Ministry of Justice, and the Executive Office of the President of Brazil) and the National Health Surveillance Agency (ANVISA). ANVISA is responsible for evaluating the quality, efficacy, and safety of all new technologies prior their sale in the Brazilian market. The agency was created during the regulatory process itself, marking the end of the 1990s and the start of the 2000s as a measure to buttress the regulatory policies implemented in Brazil's pharmaceutical market. The resumption of price regulation in the Brazilian pharmaceutical market occurred during the period in which other countries introduced reference pricing systems (Vogler, Haasis, et al. 2018).

Brazil's success with regulation of the pharmaceutical market is due to its setting of objectives based on an accurate analysis of the context in which the regulations were to be implemented. For example, at first, it sought to stabilize prices and reduce the shortages that had resulted from rising prices. It therefore introduced the rule establishing ceiling prices and annual price adjustments to control prices. The government later sought to bring domestic prices closer to international price parameters, as prices in Brazil were higher than those in the international market. This led to the introduction of the external reference pricing mechanism (ERP).

BOX 1 External reference pricing (ERP)

The WHO defines ERP as "the practice of comparing the price of pharmaceutical products in different countries to set a benchmark price." ERP is widely used, since there are significant disparities in pharmaceutical prices between countries for no apparent reason.

According to the European Commission, ERP can contribute to a substantial reduction (around 15%) in pharmaceutical prices, mainly in the short term. In the long term, the gains are usually lower, since prices tend to stabilize, generally seven to eight years after the introduction of the mechanism (Toumi, et al. 2014). Hence, it is important to combine ERP with complementary policies, such as the promotion of generics and the rational use of pharmaceuticals, to secure more affordable prices.

It should be noted that the pharmaceutical industry has been developing strategies to reduce the effectiveness of ERP. For example, it has been using a sequential launch strategy, in which pharmaceuticals are first introduced in deregulated markets or markets where they can command high prices – prices that are unrelated to research and development or production costs – with the objective of setting a parameter higher than the convergence prices in other countries. Some countries, moreover, engage in confidential negotiations of strategic products, which ends up raising the overall international price. Thus, policymakers should closely monitor the implementation of policies such as ERP to inform decision making.

3.2 HOW PRICE REGULATION WORKS IN BRAZIL

Brazil has adopted a pharmaceutical price control system under which prices are negotiated in the market based on the maximum prices set by CMED. This is the price ceiling model, in which the maximum prices are published on a list accessible to all of society on the ANVISA website, serving as a benchmark for market negotiations and public procurement.[5] Once approved for sanitary registration by ANVISA, the pharmaceutical product goes through three steps before it can be dispensed to the patient: registration for maximum price, acceptance of the pharmaceutical for use in the public sector, and price negotiation in public and private markets.

Step 1: Registration for maximum price (see Figure 6)

Before the product can be sold, the maximum permissible price of the new pharmaceutical must be registered. This is done by CMED, which sets the maximum sale price for a pharmaceutical in Brazil both for government procurement and the private market. The main regulatory instruments that CMED uses to set this maximum price are rapid health technology assessments (HTA) to compare the new pharmaceutical with products already on the market and with their prices (ERP and internal/domestic reference prices).

First, HTA is used to identify the therapeutic contribution of the new pharmaceuticals launched in the domestic market.

In Brazil, a therapeutic gain is considered to exist when:

- the new pharmaceutical product has higher efficacy than the pharmaceuticals already on the market; or
- the efficacy is maintained, and the new pharmaceutical has fewer adverse effects than the existing pharmaceuticals; or
- the efficacy is maintained, and the total cost is lower.

The results of the contribution are used in drafting the rule defining entry prices. If there is a therapeutic gain, the maximum price of the new pharmaceutical is set through external reference pricing; that is, the price will be equivalent to the lowest price found in a reference basket of 10 countries. Therefore, the ceiling for negotiating the price in the Brazilian market is the external reference price of this medicine. If there is no therapeutic gain, the price of the pharmaceutical will be the maximum equivalent to the comparator in the domestic market (internal/domestic reference price) or the lowest international price of the same 10-country basket (external reference price).

The reasoning is that **new** pharmaceutical therapies (under patent) without therapeutic gain should not have prices higher than those of existing treatments in the country in order to discourage the replacement of longstanding, inexpensive, and efficient therapies with new, inefficient, more expensive therapies. Thus, CMED puts external prices at the heart of pharmaceutical price negotiations in the country. This dynamic is displayed in the diagram in Figure 6.

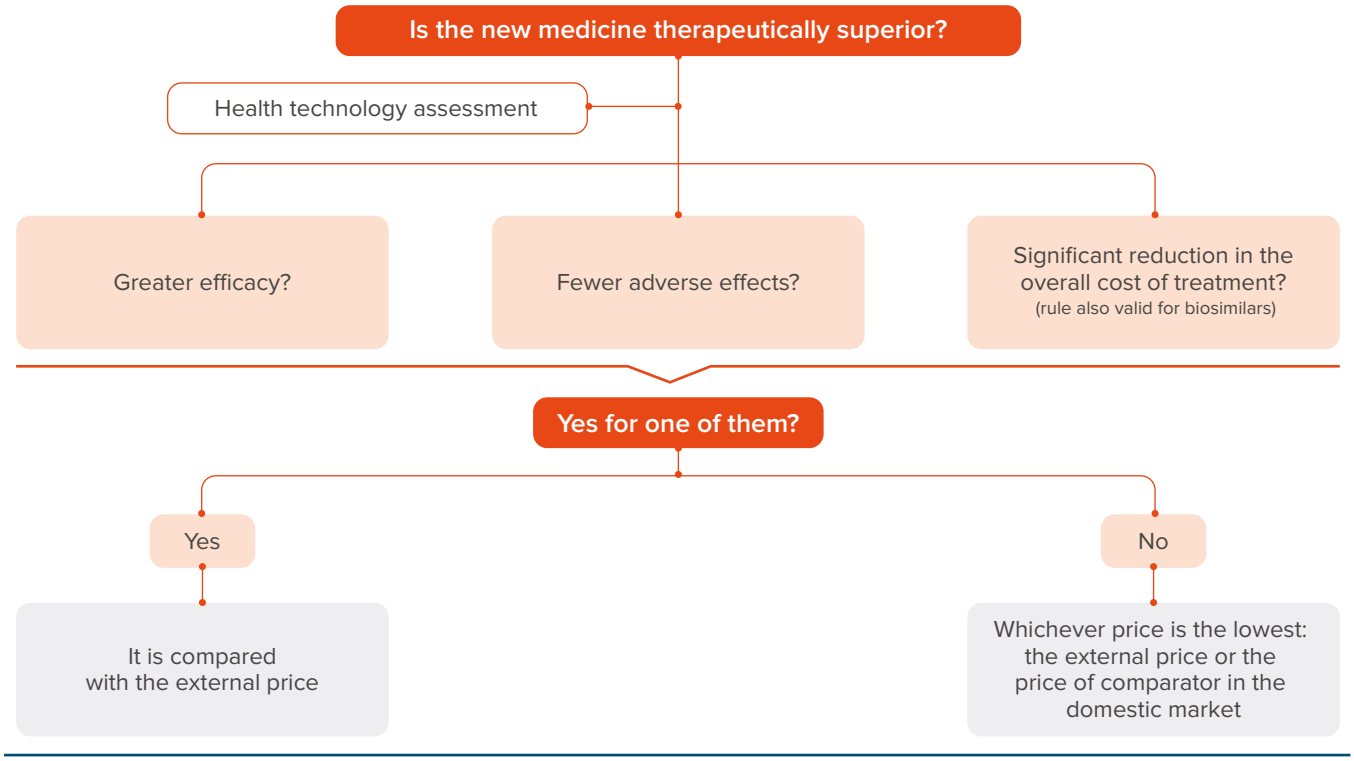
For molecules **not under patent**, price setting is based on a domestic reference system that ensures that there are no discrepancies between the prices of molecular products sold by the same company and that they do not differ from the weighted average in the market for the same molecule. Furthermore, generic products, defined in Brazil's Generics Act and policy, enter the market with a price 35% lower than the price of the innovator medicine, following the global trend to discount prices in relation to innovator pharmaceuticals.

Step 2: Acceptance of the pharmaceutical for use in the public sector (Unified Health System - SUS)

Once CMED sets the maximum price, CONITEC and similar bodies in the states assess the new pharmaceutical for eventual use in the public sector. In this process, companies propose a price for CONITEC to consider using the medicine in the SUS – a price that cannot be higher than the maximum price set by CMED in the previous step.

Based on the proposed price, CONITEC will determine whether the new pharmaceutical is more cost-effective than other therapies already used in the SUS. If it is more cost-effective, CONITEC will issue a favorable opinion to provide the new therapy in the SUS. If not, it will issue an unfavorable opinion. If the therapy is accepted for use in the SUS, the new price proposed by the company and approved by CONITEC will serve as a price ceiling for all SUS procurement of this pharmaceutical.

FIGURE 6 **Regulation of new pharmaceutical products in Brazil**



Source: Agência Nacional de Vigilância Sanitária 2004.

Step 3: Price negotiation in public and private markets

This is the final step before the pharmaceutical is available to the public. **The purchaser of the pharmaceutical in both the public and private sector will negotiate the purchase price, based on:**

- the maximum price set by CMED in step 1 for the entire Brazilian market
- the price ceiling set by CONITEC for public procurement

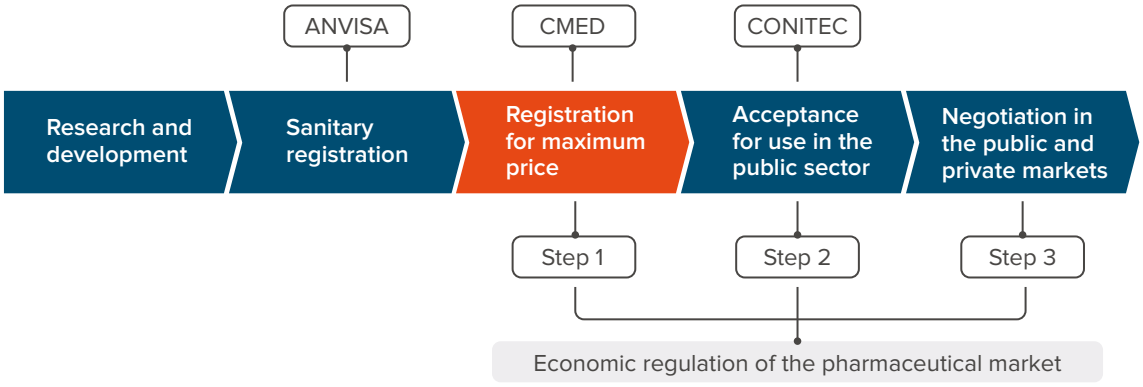
In the case of unpatented pharmaceuticals, price setting depends on the type of pharmaceutical, whether type 1, 2, or 3.

Type 1: Generics. For this type of pharmaceutical, most countries establish a compulsory discount in relation to innovative pharmaceuticals to counter the power of certain pharmaceutical firms in price setting. Brazil has opted to establish a 35% discount for the maximum price of generics (in relation to the reference pharmaceutical product). This discount is based on an estimate of the advertising expenditure for new pharmaceuticals in relation to generics. Since, in theory, there is no need to spend on advertising for generics, it was decided to impose a discount equivalent to that expense.

Type 2: Branded Generics (similar pharmaceuticals). Are medicines like generics that are not under patent but are identified by a trade name rather than the active ingredient. The maximum prices for these products cannot be higher than those of the other comparators in the company portfolio or comparators in the domestic market weighted by their market share.

Type 3: Biosimilars and biologicals. Unlike generics and similar pharmaceuticals, whose pricing is based on the maximum prices set in Brazil's regulated system, and though biosimilars and biologicals are not new pharmaceuticals, their pricing is based on the external reference price or the average market price, whichever is lower, as is the case with innovator drugs.

FIGURE 7 Steps in the regulation of new pharmaceuticals in Brazil



4. RESULTS OF REGULATION

Figure 8 **shows that a direct consequence of market deregulation in the 1990s was higher pharmaceutical prices, and that since the 2000s, there has been a significant reduction in the prices of pharmaceutical products.** Current prices in Brazil may be six times lower than in the United States.

Furthermore, since 2016 generics have been the most widely sold products by Brazil's pharmaceutical industry. At least in part, this is the result of the strategies adopted to promote this market. In 2016, of the 4.52 billion pharmaceuticals distributed by companies in this sector, 1.46 billion were generics, or 32% of the total. Some 1.42 billion were branded generics (31%). The growth of generics in the market demonstrates the success of the public policies to promote the population's access to quality medicines at more affordable prices.

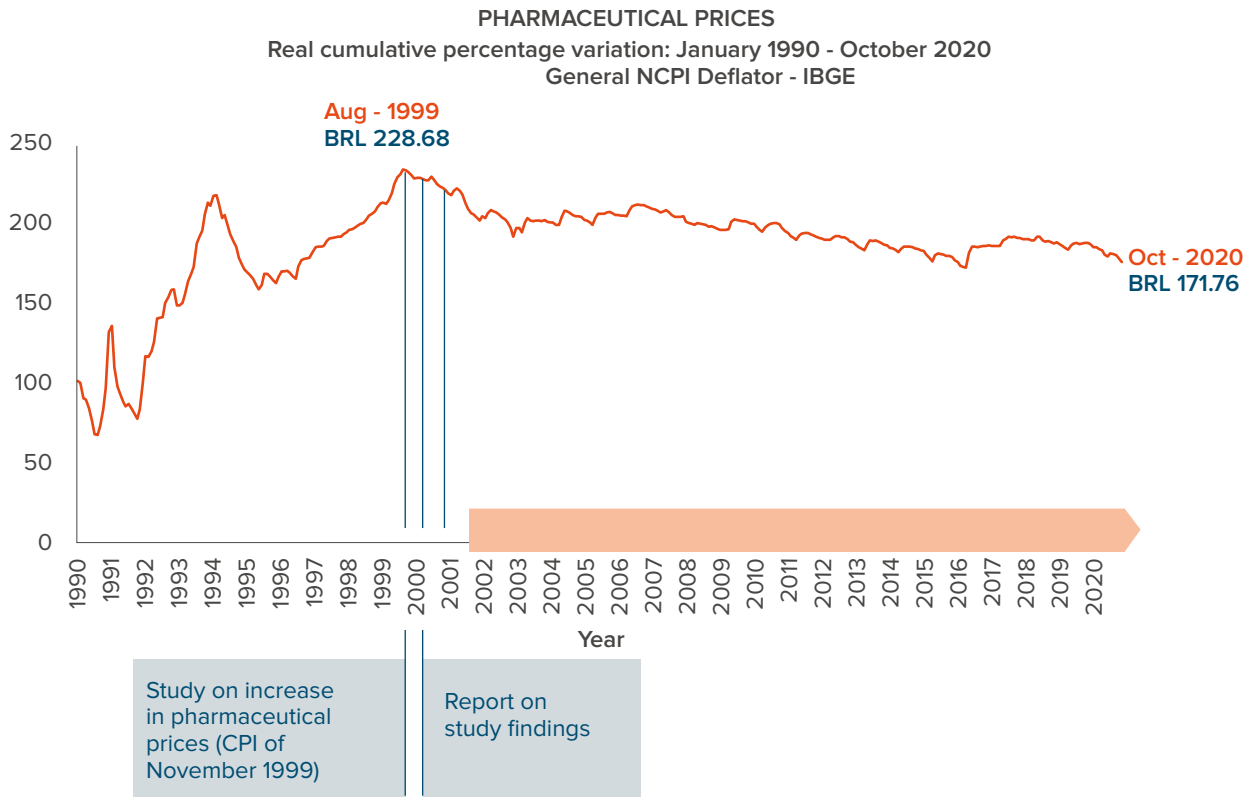
Also worth noting is the great potential of Brazil's pharmaceutical manufacturers to produce generics. In 2016, 16 of the 20 companies with the highest sales of this type of product were domestic. Three of them are public: the Oswaldo Cruz Foundation, in 8th place; Fundação para o Remédio Popular, in 16th place; and Instituto Vital Brazil, in 17th place (Agência Nacional de Vigilância Sanitária 2017).

Furthermore, there are recent examples that give an idea of the negative impacts of lack of regulation. Through a lawsuit in one case, a judicial order increased the cost of a single pharmaceutical (eculizumab), producing loses of US$178 million[6]. This was because the Ministry of Health's purchase price was higher than the one subsequently set by CMED with adequate regulation. Those resources could have been used to provide care for a large portion of the population or for the implementation of other health policies.

This was the result of direct imports without price regulation. It is also counterfactual evidence that it is uncertain whether bargaining power based on volume through centralized procurement is in itself enough to lower prices (Brazil is the most populous country in Latin America). Thus, regulatory mechanisms for price control must be introduced to complement centralized procurement. A combination of regulatory policies produces the desired result of lower pharmaceutical prices.

Pharmaceutical price inflation was much lower than overall economic inflation and half the health care inflation. From 2007 to 2017, the cumulative health care inflation was 120% – 46% higher than the average inflation in Brazil, which in that decade hovered around 82.3%. The expectation was that pharmaceutical prices would follow this trend; however, this inflation (64.9%) was not only half that of the health care one in those 10 years but remained below the general average for the country – representing a real reduction in pharmaceutical prices thanks to the regulation of the market. **Regulation of the pharmaceutical market not only controlled price variations but boosted sales, which implies an increase in access to pharmaceuticals during the period.** This persisted even during the economic crisis of 2016: contrary to expectations, sales in Brazil continued to grow in the midst of that crisis.

FIGURE 8 **Evolution of pharmaceutical prices in Brazil**



Source: ANVISA/SE-CMED, based on IBGE data (up to October 2020).

5. LESSONS LEARNED

The pharmaceutical market is characterized by major market imperfections. To overcome them, a variety of regulatory instruments can be adopted, depending on the health system, needs, and the characteristics of each country.

External reference pricing is one of the most widely used regulatory instruments, since it is efficient in the short term. To guarantee its long-term effectiveness, it is important to introduce other complementary measures.

Brazil's success with the regulation of the pharmaceutical market can be attributed to the establishment of objectives based on an accurate analysis of the country context. At first, it sought to stabilize prices and reduce shortages. To this end, it introduced a price control and annual price adjustment regulation; thus, in addition to reducing price variations, the measure increased sales, which implied greater access to pharmaceuticals during the period. This kept pharmaceutical price inflation below the national average, representing a real reduction in prices thanks to the regulation of the market. Sales continued to rise during the economic crisis of 2016, demonstrating that Brazil is an attractive market for the industry.

Finally, it is important to mention that success in regulating the pharmaceutical market does not depend solely on aligning the regulation's objectives with the regulatory instruments. It is also essential to improve price monitoring mechanisms, domestic legislation, and other complementary policies such as promoting the use of generics and parallel imports.

GLOSSARY

ERP	External reference pricing
CMED	Brazilian Pharmaceutical Market Regulation Chamber
ANVISA	Brazilian Health Regulatory Agency
CONITEC	Brazilian National Committee for Technology Incorporation
SUS	Brazilian Unified Health System

NOTES

[1] The concept of "credentialed products" was developed by Darby and Karni (1973) and applied in the 2001 study of Brazil's pharmaceutical industry by Fiuza, Eduardo and Lisboa, Marcos. "*Some aspects of the quality of a good may never be subject to evaluation by the consumer; these goods are called credentialed goods, since only a specialized professional can attest to these aspects, certifying the goods*", free translation (Fiuza and Lisboa 2001).

[2] Brand loyalty: the patient is motivated to continue using a specific brand of pharmaceutical, either because he has derived some clinical benefit from it, or he believes that the price is appropriate. Degree of differentiation unknown to the consumer: differentiating a pharmaceutical is a competitive strategy designed to make the consumer believe that a certain brand of the product is different from that of the competition. It is based on variety (horizontal differentiation) in color, size, texture, or quality (vertical differentiation).

[3] For a graphic representation of this concept and more detailed description of measures to regulate price and volume, see Breve 11: "Value Based Pharmaceutical Reimbursement: Introduction to the Main Features of the German Pharmaceutical Policy", based on a presentation by Dr. Wolfgang Greiner (BID 2016).

[4] To learn more about other pharmaceutical policy strategies, view Red CRITERIA's webinar series, especially the webinars of Wirtz, Bardey, and Durán (2019), Vaca (2019), Vogler (2018), and Bañuelos (2016).

[5] The list of maximum permissible prices in the Brazilian market is available for consultation at https://www.gov.br/anvisa/pt-br/assuntos/medicamentos/cmed/precios.

[6] Comparison of purchase prices by the Ministry of Health, published in https://governodigital.net/ and maximum prices permitted in CMED, published in https://www.gov.br/anvisa/pt-br/assuntos/medicamentos/cmed/precos, multiplied by the amount procured.

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